Remarks

Claim 31 remains pending.

Rejections Under 35 U.S.C. § 103

In the Office Action, claim 31 has been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over

(i) Arnon (U.S. Pat. No. 5,562,907) in view of Borodic et al. (1993) or Schantz et al. (1992), or Wilson et al. (1982);

(ii) Graham (U.S. Pat. Pub. No. 2002/0102275) in view of Arnon, Borodic et al. or Schantz et al., or Wilson et al;

(iii) Johnson et al. (U.S. Pat. No. 5,696,077) in view of Elston et al. (1985), further in view of Borodic et al. or Schantz et al. or Wilson et al.;

(iv) Johnson et al. in view of Arnon;

(v) Elston et al. in view of Borodic et al. or Schantz et al. or Wilson et al.; and

(vi) Elston et al. in view of Arnon.

Applicant respectfully traverses the rejections.

The Office Action indicates that applicant has not presented arguments why claim 31 is patentable over the above rejections. Applicant disagrees.

In the response filed on September 30, 2003, applicant traversed the rejections under 35 U.S.C. § 103(a) and in support of the traversal referred to the February 8, 2001 declaration of Dr. Mitchell Brin (hereinafter the Brin Declaration), which was submitted with the application as originally filed, as evidence

supporting the unobviousness and patentability of the present claim. The Examiner appears to have not taken into consideration the evidence presented by way of the Brin Declaration.

The Brin Declaration Rebuts the Obviousness Rejection

A copy of the Brin Declaration is being submitted with this response.

Decisions from the courts, which review patent office decisions, are instructive as to the deference and weight to be accorded the evidence presented in the Brin Declaration. An expert opinion expressed in a Declaration can overcome an obviousness rejection: "The expert opinion was introduced on the issue of the level of ordinary skill … the prima facie case of obviousness has been overcome", and the Examiner's obviousness rejection was reversed. *In re Oelrich and Divigard*, 579 F.2d 86, 198 USPQ 210 at 215 (CCPA 1978).

Additionally, in *In re May and Eddy*, 574 F.2d, 197 USPQ 601 (CCPA 1978), four declarations were submitted in response to an obviousness rejection. The Court relied heavily upon the affidavit from an expert in the field (the Jackson affidavit) which stated that the claimed method of affecting analgesic and morphine antagonistic activity through use of a particular compound "was unexpected and unpredictable" since the property of the compound used in the method to affect analgesic and morphine antagonistic activity "had not previously been established." (197 USPQ at 606) (emphasis added). The Court concluded based in large part upon the Jackson affidavit (see

197 USPQ 608, paragraph [6]) that the method claims were not obvious, and reversed the Examiner's obviousness rejection. *In re May and Eddy* is directly applicable here since the present claims are method claims (treatment of strabismus), which use a particular compound (botulinum toxin type B).

The original of the Brin declaration was submitted in related U.S. Application Serial Number 09/490,756 with the response dated February 16, 2001. Dr. Brin is an acknowledged expert in the use of botulinum toxin for treating neuromuscular disorders.

Paragraph 6 of the Brin declaration states: "As of the April 25, 1991 date of the Jankovic reference, it was **completely unknown** as to whether or not botulinum toxin type B would have any therapeutic efficacy in humans. Indeed, as far as I am aware, the first reported use of type B botulinum toxin in humans did not occur until 1995" (emphasis added).

Additionally, paragraph 8 of the Brin declaration states: "In my opinion, prior to December 28, 1993, it would have been **foolhardy and dangerous** to use botulinum toxin type B to treat patients with dystonia, such as cervical dystonia, in light of clinical experience with the type B toxin as of that date" (emphasis added).

The Brin declaration has been submitted as evidence that the claims in this application are in condition for allowance, that is that the claims are unobvious from and patentable over the prior art. In other words, since there had been no use of botulinum toxin type B to treat any disease condition prior to

the effective filing date of the present application (i.e., December 28, 1993) and based upon the additional evidence presented by the Brin declaration, the present claim (claim 31), directed to the use of botulinum toxin type B to treat strabismus, is free of the art and is in condition for allowance.

Note that as set forth in the Brin declaration, the first reported use of botulinum toxin type B (to which the present claim is directed) to treat any ailment was not until 1995. Hence, it follows that it would have been **"foolhardy and dangerous"** to use botulinum toxin type B to treat strabismus in a patient prior to the December 28, 1993 effective filing date of the instant application.

In view of the above, applicant submits that the present claim is unobvious and patentable over the prior art as cited in the Office Action.

In addition, applicant submits that a *prima facie* case of obviousness has not been established because the Office Action fails to indicate where in the prior art a suggestion or motivation is provided to combine the references, and how such a combination teaches or suggests all of the elements of the present claims.

For example, Arnon is not prior art to the above identified patent application and the presently claimed invention.

Arnon (the '907 patent) was filed on June 6, 1994 as a continuation-in-part of U.S. Application No. 08/062,110 (the

'110 application), filed on May 14, 1993. As discussed herein, the disclosure in the '907 patent relied upon by the Examiner in the December 24, 2003 Office Action was new matter that was added to the '110 application via the continuation-in-part application, which is now the '907 patent. For example, the portion at column 1, lines 35-42 is not present in the '110 application. This language is provided below:

> Botulinum toxin produces muscle paralysis and relaxation by blocking the motoneuron from releasing acetylcholine at the neuromuscular junction. This effect derives from the enzymatic action of the "light" (50,000 MW) chain of botulinum toxin, the various types (A-G) of which hydrolyze key proteins which the motoneuron relies on for the release of the acetylcholine-containing vesicles that trigger muscle contraction.

Accordingly, this disclosure in the '907 patent is **not** entitled to the May 14, 1993 priority date, and thus, this disclosure has an **effective filing date of June 6, 1994**. Because the instant application has an effective filing date of December 28, 1993, the instant application predates the disclosure identified in the Office Action. Accordingly, the **'907 patent is not prior art** with respect to the claimed invention.

In addition, applicant submits that Arnon is directed to the use of an anti-toxin in conjunction with botulinum toxin therapy. Arnon's discussion of existing strabismus treatments are only directed to botulinum toxin type A. Applicant submits that Arnon does not disclose, teach, or even suggest the administration of botulinum toxin type B to treat strabismus, as recited in the present claims.

Regarding the rejections over Wilson et al. (1982), applicant submits that Wilson et al. does not disclose, teach, or suggest the present invention. For example, Wilson et al. does not disclose, teach, or even suggest administering any type of botulinum toxin, let alone botulinum toxin type B, to a patient to treat strabismus, as recited in the present claims. Wilson et al. discusses the multiple, widespread and diverse symptoms of type B botulism, which occurs upon inadvertent intoxication (systemic poisoning) of a person with a large amount of botulinum toxin. Contrary to the Examiner's opinion, Wilson et al. does not provide any indication, let alone a disclosure, teaching, or suggestion, that botulinum toxin type B would serve to reduce muscle spasm with greater potency than type A. Thus, applicant submits that Wilson et al. does not provide any disclosure, teaching, or suggestion that would make the present claim obvious to a person of ordinary skill in the art.

Regarding the rejections over Borodic et al., applicant submits that Borodic et al. does not disclose, teach, or suggest the present invention. Borodic et al. actually identifies several significant differences between botulinum toxin type A and type B (e.g., see discussion). Borodic et al. provides no disclosure, teaching, or even a suggestion that botulinum toxin type B may be administered to a patient to treat strabismus.

Regarding the rejections over Graham, applicant submits that Graham does not specifically disclose, teach, or suggest the present invention. For example, Graham does not specifically disclose, teach, or even suggest, the use of any

botulinum toxin, let alone botulinum toxin type B, to treat strabismus. Graham discloses the use of botulinum toxin to treat juvenile cerebral palsy, which is condition entirely different and distinct from strabismus.

Regarding the rejection over Johnson, applicant submits that Johnson does not disclose, teach, or suggest the present invention. Johnson discloses a botulinum toxin type B formulation to generally treat muscular disorders. Johnson does not identify or even suggest strabismus of one of the types of disorders to be treated. In addition, Johnson does not provide a suggestion or motivation that would make obvious to a person of ordinary skill in the art that the administration of botulinum toxin type B could be used to treat strabismus.

Regarding the rejections over Elston et al., applicant submits that Elston et al. does not disclose, teach, or suggest the present invention. For example, Elston et al. does not disclose, teach, or even suggest the administration of botulinum toxin type B to treat strabismus. The entire disclosure of Elston et al. relates solely to the administration of botulinum toxin type A to treat strabismus. In addition, Elston et al. does not provide a suggestion or motivation that would make obvious to a person of ordinary skill in the art that the administration of botulinum toxin type B could be used to treat strabismus.

In view of the above, applicant submits that the present claim, that is claim 31, is unobvious from and patentable over the references, taken alone or in any combination, under 35 U.S.C. § 103.

In conclusion, applicant has shown that the present claim is not anticipated by and are unobvious from and patentable over the prior art under 35 U.S.C. §§ 102 and 103. Therefore, applicant submits that the present claim, that is claim 31 is allowable. Therefore, applicant respectfully requests the Examiner to pass the above-identified application to issuance at an early date. Should any matters remain unresolved, the Examiner is requested to call (collect) applicant's attorney at the telephone number given below.

Respectfully submitted,

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